PROSITE: a dictionary of sites and patterns in proteins

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Background

PROSITE is a compilation of sites and patterns found in protein sequences. The use of protein sequence patterns (or motifs) to determine the function of proteins is becoming very rapidly one of the essential tools of sequence analysis. This reality has been recognized by many authors [1,2]. While there have been a number of recent reports [3,4] that review published patterns, no attempt had been made until very recently [5,6] to systematically collect biologically significant patterns or to discover new ones. It is for these reasons that we have developed, since 1988, a dictionary of sites and patterns which we call PROSITE.

Some of the patterns compiled in PROSITE have been published in the literature, but the majority have been developed, in the last two years, by the author.

Format

The PROSITE database is composed of two ASCII (text) files. The first file (PROSITE.DAT) is a computer-readable file that contains all the information necessary to programs that make use of PROSITE to scan sequence(s) with pattern(s). This file also includes, for each of the patterns described, statistics on the number of hits obtained while scanning for that pattern in the SWISS-PROT protein sequence data bank [7]. Cross-references to the corresponding SWISS-PROT entries are also present in that file. The second file (PROSITE.DOC), which we call the textbook, contains textual information that documents each pattern. A user manual (PROSUSER.TXT) is distributed with the database, it fully describes the format of both files. A sample textbook entry is shown in Figure 1 with the corresponding data from the pattern file.

Leading concepts

The design of PROSITE follows four leading concepts:

Completeness. For such a compilation to be helpful in the determination of protein function, it is important that it contains a significant number of biologically meaningful patterns.

High specificity of the patterns. In the majority of cases we have chosen patterns that are specific enough not to detect too many unrelated sequences, yet that detect most if not all sequences that clearly belong to the set in consideration.

Documentation. Each of the patterns is fully documented; the documentation includes a concise description of the family of protein that it is supposed to detect as well as an explanation on the reasons that led to the selection of the particular pattern.

Periodic reviewing. It is important that each pattern be periodically reviewed, so as to insure that it is still relevant.

Content of the current release

Release 6.10 of PROSITE (February 1991) contains 375

documentation entries describing 433 different patterns. The list of these entries is provided in Appendix 1.

Distribution

PROSITE is distributed on magnetic tape and on CD-ROM by the EMBL Data Library. For all enquiries regarding the subscription and distribution of PROSITE one should contact:

EMBL Data Library European Molecular Biology Laboratory Postfach 10.2209, Meyerhofstrasse 1 6900 Heidelberg, Germany

Telephone: (+49 6221) 387 258

Telefax: (+49 6221) 387 519 or 387 306

Electronic network address: DATALIB@EMBL.BITNET

PROSITE can be obtained from the EMBL File Server [8]. Detailed instructions on how to make best use of this service, and in particular on how to obtain PROSITE, can be obtained by sending to the network address NETSERV@EMBL.BITNET the following message:

HELP HELP PROSITE

If you have access to a computer system linked to the Internet you can obtain PROSITE using FTP (File Transfer Protocol), from the following file servers:

GenBank On-line Service [9]

Internet address: genbank.bio.net (134.172.1.160)

NCBI

Internet address: ncbi.nlm.nih.gov (130.14.20.1)

The present distribution frequency is four releases per year. No restrictions are placed on use or redistribution of the data.

REFERENCES

- 1. Doolittle R.F. (In) Of URFs and ORFs: a primer on how to analyze derived amino acid sequences., University Science Books, Mill Valley, California,
- 2. Lesk A.M. (In) Computational Molecular Biology, Lesk A.M., Ed., pp17-26, Oxford University Press, Oxford (1988).
- Barker W.C., Hunt T.L., George D.G. Protein Seq. Data Anal. 1:363-373(1988).
- 4. Hodgman T.C. CABIOS 5:1-13(1989).
- 5. Bork P. FEBS Lett. 257:191-195(1989).
- 6. Smith H.O., Annau T.M., Chandrasegaran S. Proc. Natl. Acad. Sci. USA 87:826-830(1990).
- Bairoch A., Boeckmann B. Nucleic Acids Res. 19:2247-2249(1991).
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- 9. Benton D. Nucleic Acids Res. 18:1517-1520(1990).

1a) A documentation (textbook) entry

Replicative DNA polymerases (EC 2.7.7.7) are the key enzymes catalyzing the accurate replication of DNA. They require either a small RNA molecule or a protein as a primer for the de novo synthesis of a DNA chain. On the basis of sequence similarities a number of DNA polymerases have been grouped together [1 to 5] under the designation of DNA polymerase family B. The polymerases that belong to this family are:

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- Human polymerase alpha.

Yeast polymerase I, polymerase III, and polymerase REV3.

Polymerases of viruses from the herpesviridae family (Herpes type I and II, Epstein-Barr, Cytomegalovirus, and Varicella-zoster).

Polymerases from Adenoviruses.

Polymerases from Baculoviruses.

Vaccinia virus polymerase.

Bacteriophage T4 polymerase.

Podoviridae bacteriophages Phi-29, M2, and PZA polymerase.

Tectiviridae bacteriophage PRD1 polymerase.

Putative polymerases from yeast K. lactis linear plasmids pGKL1 and pGKL2.

Putative polymerase from the maize mitochondrial plasmid-like S1 DNA.
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Six regions of similarity (numbered from I to VI) are found in all or a subset of the above polymerases. The most conserved region (I) includes a perfectly conserved tetrapeptide which contains two aspartate residues. The function of this conserved region is not yet known, however it has been suggested [3] that it may be involved in binding a magnesium ion. We use this conserved region as a signature for this family of DNA polymerases.

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- Consensus pattern: [YA]-x-D-T-D-S-[LIVMT]
- Sequences known to belong to this class detected by the pattern: ALL.
- Other sequence(s) detected in SWISS-PROT: chicken vitellogenin 2.
- Note: the residue in position 1 is Tyr in every family B polymerases, except in phage T4, where it is Ala.
- Last update: February 1991 / Text revised.

[1] Jung G., Leavitt M.C., Hsieh J.-C., Ito J.
Proc. Natl. Acad. Sci. U.S.A. 84:8287-8291(1987).

[2] Bernad A., Zaballos A., Salas M., Blanco L.
EMBO J. 6:4219-4225(1987).

[3] Argos P.
Nucleic Acids Res. 16:9909-9916(1988).

[4] Wang T.S.-F., Wong S.W., Korn D.
FASEB J. 3:14-21(1989).

[5] Delarue M., Poch O., Todro N., Moras D., Argos P.
Protein Engineering 3:461-467(1990).

(END)
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1b) The corresponding entry in the pattern file

Figure 1. Sample data from PROSITE

Appendix 1. List of patterns documentation entries in release 6.10 of PROSITE

Post-translational modifications

N-glycosylation site

Glycosaminoglycan attachment site

Tyrosine sulfatation site

cAMP- and cGMP-dependent protein kinase phosphorylation site

Protein kinase C phosphorylation site Casein kinase II phosphorylation site Tyrosine kinase phosphorylation site

N-myristoylation site

Amidation site

Aspartic acid and asparagine hydroxylation site Vitamin K-dependent carboxylation domain

Phosphopantetheine attachment site

Prokaryotic membrane lipoprotein lipid attachment site

Farnesyl group binding site (CAAX box)

Domains

Endoplasmic reticulum targeting sequence

Peroxisomal targeting sequence

Gram-positive cocci surface proteins 'anchoring' hexapeptide

Nuclear targeting sequence

Cell attachment sequence

ATP/GTP-binding site motif A (P-loop)

EF-hand calcium-binding domain

Actinin-type actin-binding domain signatures

Cofilin/tropomyosin-type actin-binding domain

Kringle domain signature

EGF-like domain cysteine pattern signature

Type II fibronectin collagen-binding domain

Hemopexin domain signature 'Trefoil' domain signature

Chitin recognition or binding domain signature

WAP-type 'four-disulfide core' domain signature

DNA or RNA associated proteins

'Homeobox' domain signature 'Homeobox' antennapedia-type protein signature

'Homeobox' engrailed-type protein signature

'Paired box' domain signature

'POU' domain signature

Zinc finger, C2H2 type, domain

Nuclear hormones receptors DNA-binding region signature

Eryf1-type zinc finger domain

Poly(ADP-ribose) polymerase zinc finger domain

Leucine zipper pattern

Fos/jun DNA-binding basic domain signature

Myb DNA-binding domain repeat signatures

Myc-type, 'helix-loop-helix' putative DNA-binding domain signature

p53 tumor antigen signature

'Cold-shock' DNA-binding domain signature

CTF/NF-I signature

ETS-domain signatures

SRF-type transcription factors DNA-binding and dimerization domain

Transcription factor TFIID repeat signature

eIF-4A family ATP-dependent helicases signatures

Eukaryotic putative RNA-binding region RNP-1 signature Bacterial activator proteins, araC family signature

Bacterial activator proteins, crp family signature

Bacterial activator proteins, gntR family signature

Bacterial activator proteins, lacI family signature

Bacterial activator proteins, lysR family signature Bacterial histone-like DNA-binding proteins signature

Histone H2A signature

Histone H2B signature

Histone H3 signature

Histone H4 signature

HMG1/2 signature

HMG-I and HMG-Y DNA-binding domain (A+T-hook)

HMG14 and HMG17 signature

Protamine P1 signature

Ribosomal protein L5 signature

Ribosomal protein L11 signature

Ribosomal protein L14 signature

Ribosomal protein L23 signature

Ribosomal protein L39/L46 signature

Ribosomal protein S7 signature

Ribosomal protein S8 signature

Ribosomal protein S9 signature

Ribosomal protein S10 signature

Ribosomal protein S11 signature

Ribosomal protein S12 signature

Ribosomal protein S15 signature

Ribosomal protein S17 signature

Ribosomal protein S18 signature

Ribosomal protein S19 signature

DNA mismatch repair proteins mutL / hexB / PMS1 signature

Enzymes

Oxidoreductases

Zinc-containing alcohol dehydrogenases signature

Iron-containing alcohol dehydrogenases signature

Insect-type alcohol dehydrogenase / ribitol dehydrogenase family signature

Aldo/keto reductase family signatures

L-lactate dehydrogenase active site

Glycerate-type 2-hydroxyacid dehydrogenases signature

Hydroxymethylglutaryl-coenzyme A reductases signatures

3-hydroxyacyl-CoA dehydrogenase signature

Malate dehydrogenase active site signature

Malic enzymes signature

Glucose-6-phosphate dehydrogenase active site

Bacterial quinoprotein dehydrogenases signatures

Aldehyde dehydrogenases active site

Glyceraldehyde 3-phosphate dehydrogenase active site

Acyl-CoA dehydrogenases signatures

Glutamate dehydrogenases active site Dihydrofolate reductase signature

Pyridine nucleotide-disulphide oxidoreductases active site

Nitrite reductases and sulfite reductase putative siroheme-binding sites

Uricase signature

Cytochrome c oxidase subunit I, copper B binding region signature

Cytochrome c oxidase subunit II, copper A binding region signature

Multicopper oxidases signatures

Lipoxygenases, putative iron-binding region signature

Extradiol ring-cleavage dioxygenases signature

Intradiol ring-cleavage dioxygenases signature

Biopterin-dependent aromatic amino acid hydroxylases signature

Copper type II, ascorbate-dependent monooxygenases signatures

Cytochrome P450 cysteine heme-iron ligand signature

Copper/Zinc superoxide dismutase signature Manganese and iron superoxide dismutases signature

Ribonucleotide reductase large subunit signature

Ribonucleotide reductase small subunit signature

Nitrogenases component 1 alpha and beta subunits signature

Transferases

Thymidylate synthase active site

Methylated-DNA--protein-cysteine methyltransferase active site

N-6 Adenine-specific DNA methylases signature

N-4 cytosine-specific DNA methylases signature

C-5 cytosine-specific DNA methylases signatures

Serine hydroxymethyltransferase pyridoxal-phosphate attachment site

Phosphoribosylglycinamide formyltransferase active site Aspartate and ornithine carbamoyltransferases signature

Thiolases signatures

Chloramphenicol acetyltransferase active site

cysE / lacA / nodL acetyltransferases signature

Phosphorylase pyridoxal-phosphate attachment site

UDP-glucoronosyl and UDP-glucosyl transferases signature Purine/pyrimidine phosphoribosyl transferases signature

S-Adenosylmethionine synthetase signatures

EPSP synthase active site Aspartate aminotransferases pyridoxal-phosphate attachment site

Hexokinases signature

Galactokinase signature

Phosphofructokinase signature Protein kinases signatures

Pyruvate kinase active site signature

Phosphoglycerate kinase signature

Aspartokinase signature

ATP:guanido phosphotransferases active site

PTS proteins phosphorylation sites signatures

Adenylate kinase signature

Phosphoribosyl pyrophosphate synthetase signature

Eukaryotic RNA polymerase II heptapeptide repeat

DNA polymerase family B signature

Galactose-1-phosphate uridyl transferase active site signature

CDP-alcohol phosphatidyltransferases signature

Rhodanese active site

Hydrolases

Phospholipase A2 active sites signatures

Lipases, serine active site

Colipase signature

Carboxylesterases type-B active site

Alkaline phosphatase active site

Fructose-1 – 6-bisphosphatase active site

Serine/threonine specific protein phosphatases signature

Tyrosine specific protein phosphatases active site
Prokaryotic zinc-dependent phospholipase C signature

3'5'-cyclic nucleotide phosphodiesterases signature

Sulfatases signature

Pancreatic ribonuclease family signature

Alpha-lactalbumin / lysozyme C signature

Lysosomal alpha-glucosidase / sucrase-isomaltase active site

Alpha-L-fucosidase putative active site

Uracil-DNA glycosylase signature

Serine carboxypeptidases, serine active site

Zinc carboxypeptidases, zinc-binding regions signatures

Serine proteases, trypsin family, active sites Serine proteases, subtilisin family, active sites

ClpP proteases active sites

Eukaryotic thiol (cysteine) proteases active site

Ubiquitin carboxyl-terminal hydrolase, putative active-site signature

Eukaryotic aspartyl proteases active site

Neutral zinc metallopeptidases, zinc-binding region signature

Insulin-degrading enzyme / E.coli protease III signature

recA signature

Proteasome subunits signature

Asparaginase / glutaminase signature

Urease active site

Beta-lactamases classes -A, -C, and -D active site

Arginase and agmatinase signatures

Inorganic pyrophosphatase signatures

Acylphosphatase signatures

ATP synthase alpha and beta subunits signature

ATP synthase gamma subunit signature

ATP synthase delta (OSCP) subunit signature

E1-E2 ATPases phosphorylation site

Sodium and potassium ATPases beta subunits signatures

Cutinase, serine active site

Lvases

DDC / GAD / HDC pyridoxal-phosphate attachment site

Orotidine 5'-phosphate decarboxylase signature

Phosphoenolpyruvate carboxylase active site

Ribulose bisphosphate carboxylase large chain active site

Fructose-bisphosphate aldolase active site

KDPG and KHG aldolases active site signatures

Isocitrate lyase signature

DNA photolyases signature

Carbonic anhydrases signature

Fumarate lyases signature

Enolase signature

Serine/threonine dehydratases pyridoxal-phosphate attachment site

Enoyl-CoA hydratase signature

Tryptophan synthase alpha chain signature

Tryptophan synthase beta chain pyridoxal-phosphate attachment site

Delta-aminolevulinic acid dehydratase active site

Isomerases

Alanine racemase pyridoxal-phosphate attachment site

Peptidyl-prolyl cis-trans isomerase signature

Triosephosphate isomerase active site

Xvlose isomerase signatures

Phosphoglucose isomerase signature

Phosphoglycerate mutase family phosphohistidine signature

Eukarvotic DNA topoisomerase I active site

Prokaryotic DNA topoisomerase I active site

DNA topoisomerase II signature

Ligases

Aminoacyl-transfer RNA synthetases class-I signature Aminoacyl-transfer RNA synthetases class-II signatures

ATP-citrate lyase and succinyl-CoA ligases active site

Glutamine synthetase signatures

Ubiquitin-conjugating enzymes active site

Phosphoribosylglycinamide synthetase signature

ATP-dependent DNA ligase putative active site

Others enzymes

Isopenicillin N synthetase signatures

Site-specific recombinases signatures

Thiamine pyrophosphate enzymes signature

Biotin-requiring enzymes attachment site

2-oxo acid dehydrogenases acyltransferase component lipoyl binding site

Electron transport proteins

Cytochrome c family heme-binding site signature

Cytochrome b5 family, heme-binding domain signature

Cytochrome b/b6 signatures

Thioredoxin family active site

Glutaredoxin active site

Type-1 copper (blue) proteins signature

2Fe-2S ferredoxins, iron-sulfur binding region signature

4Fe-4S ferredoxins, iron-sulfur binding region signature

Rieske iron-sulfur protein signatures

Flavodoxin signature

Rubredoxin signature

Other transport proteins

Class I metallothioneins signature

Ferritin iron-binding region signature

Transferrins signatures

Plant hemoglobins signature

Arthropod hemocyanins / insect LSPs signatures

ATP-binding proteins 'active transport' family signature

Binding-protein-dependent transport systems inner membrane component signature

Serum albumin family signature

Lipocalins signature

Cytosolic fatty-acid binding proteins signature

LBP / BPI / CETP family signature

Uteroglobin family signatures

Mitochondrial energy transfer proteins signature

Sugar transport proteins signatures

Prokaryotic sulfate-binding proteins signature

Amino acid permeases signature

Anion exchangers family signatures MIP / Nodulin-26 / glpF family signature

Insulin-like growth factor binding proteins signature

Structural proteins

43 Kd postsynaptic protein signature

Actins signatures

Annexins phospholipid/calcium-binding domain signature

Clathrin light chain signature

Connexins signatures

Crystallins beta and gamma 'Greek key' motif signature

Dynamin family signature

Intermediate filaments signature

Kinesin motor domain signature

Neuromodulin (GAP-43) signatures Profilin signature

Surfactant associated polypeptide SP-C palmytoylation sites Synapsins signatures Synaptobrevin signature Tropomyosins signature Tubulin subunits alpha and beta signature Tubulin-beta mRNA autoregulation signal Tau and MAP2 proteins repeated region signature Neuraxin and MAP1B proteins repeated region signature F-actin capping protein beta subunit signature Amyloidogenic glycoprotein signatures Cadherins extracellular repeated domain signature Insect larval cuticle proteins signature Gas vesicles protein GVPa signature Gas vesicles protein GVPc repeated domain signature

Receptors

NMePhe pili methylation site

Neurotransmitter-gated ion-channels signature G-protein coupled receptors signature Visual pigments (opsins) retinal binding site Bacterial rhodopsins retinal binding site Receptor tyrosine kinase class II signature Receptor tyrosine kinase class III signature Growth factor and cytokines receptors family signature Integrins alpha chain signature Integrins beta chain cysteine-rich domain signature Photosynthetic reaction center proteins signature Photosystem I psaA and psaB proteins signature Phytochrome chromophore attachment site Speract receptor repeated domain signature TonB-dependent receptor proteins signatures Type-II membrane antigens family signature

Potexviruses and carlaviruses coat protein signature

Cytokines and growth factors

Int-1 family signature HBGF/FGF family signature Nerve growth factor family signature Platelet-derived growth factor (PDGF) family signature TGF-beta family signature TNF family signature Interferon alpha and beta family signature Interleukin-1 signature Interleukin-2 signature Interleukin-6 / G-CSF / MGF signature Interleukin-7 signature

Hormones and active peptides

Adipokinetic hormone family signature Bombesin-like peptides family signature Calcitonin / CGRP / IAPP family signature Chromogranins / secretogranins signatures Gastrin / cholecystokinin family signature Glucagon / GIP / secretin / VIP family signature Glycoprotein hormones beta chain signature Insulin family signature Natriuretic peptides signature Neurohypophysial hormones signature Pancreatic hormone family signature Parathyroid hormone family signature Somatotropin, prolactin and related hormones signatures Tachykinin family signature Cecropin family signature Mammalian defensins signature Insect defensins signature Endothelins / sarafotoxins signature

Toxins

Plant thionins signature Snake toxins signature Heat-stable enterotoxins signature Aerolysin type toxins signature Shiga/ricin ribosomal inactivating toxins active site signature Channel forming colicins signature Staphyloccocal enterotoxins / Streptococcal pyrogenic exotoxins signatures Membrane attack complex components / perforin signature

Inhibitors

Pancreatic trypsin inhibitor (Kunitz) family signature Bowman-Birk serine protease inhibitors family signature Kazal serine protease inhibitors family signature Soybean trypsin inhibitor (Kunitz) protease inhibitors family signature Serpins signature Potato inhibitor I family signature Squash family of serine protease inhibitors signature Cysteine proteases inhibitors signature Tissue inhibitors of metalloproteinases signature Cereal trypsin/alpha-amylase inhibitors family signature Disintegrins signature

Others Pentraxin family signature Immunoglobulins and major histocompatibility complex proteins signature Prion protein signature Cyclin signature Proliferating cell nuclear antigen signature Arrestins signature Chaperonins signature Heat shock hsp70 proteins family signatures Heat shock hsp90 proteins family signature Ubiquitin signature SRP54-type proteins GTP-binding domain signature GTP-binding elongation factors signature Eukaryotic initiation factor 4D hypusine signature S-100/ICaBP type calcium binding protein signature Hemolysin-type putative calcium-binding region signature Small, acid-soluble spore proteins, alpha/beta type, signature Caseins alpha/beta signature

Legume lectins signatures Vertebrate galactoside-binding lectin signature Lysosome-associated membrane glycoproteins signatures Glycophorin A signature Seminal vesicle protein I repeats signature HCP repeats signature Bacterial ice-nucleation proteins octamer repeat Cell cycle proteins ftsW / rodA / spoVE signature Staphylocoagulase repeat signature 11-S plant seed storage proteins signature Dehydrins signature Small hydrophilic plant seed proteins signature Thaumatin family signature